

REMARKS/ARGUMENTS

I. Status of the claims

Claim 31 is amended. Claims 15-17, 23-26, and 31-41 are pending.

Support for the amendment can be found in the first full paragraph of page 25.

No new matter is added.

II. Rejection under 35 U.S.C. § 103

A. Claims 15-16, 23-26, 31-35, and 38-41

The Examiner rejected claims 15-16, 23-26, 31-35, and 38-41 as allegedly obvious in view of Lowe *et al.* over Zhang *et al.* Specifically, the Examiner argued that Lowe *et al.* taught all of the limitations of the rejected claims except for the step of determining a non-linear continuously differentiable function of a logarithm of copy number. However, the Examiner argued that Zhang *et al.* taught a step of calculating the logarithm of copy number in relation to a references nucleic acid and that those of skill in the art would have been motivated to combine that step with the methods of Lowe *et al.*

Applicants respectfully traverse the rejection because the Examiner has not set forth a *prima facie* case of obviousness. A proper *prima facie* case of obviousness requires that the Examiner establish: 1) that the elements of the claimed invention are in the prior art, 2) that there is a motivation to combine the elements as claimed, and 3) that there is an objective reason why those of skill in the art would have had a reasonable expectation that the combined elements function as intended. See MPEP § 2143; *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991).

The cited references do not describe all of the elements of the present claims.

The Examiner states that "Lowe *et al.* did not teach determining a non-linear ... function of a logarithm of a copy number" (Office Action, page 4), but then does not explain how Zhang *et al.* teaches the use of non-linear functions. The only portion of Zhang *et al.* specifically referred to in the Office Action is column 9, lines 7-36. That section states that a correlation between threshold cycle and initial DNA concentration can be determined, but does

not teach what that relationship is. No where does Zhang *et al.* teach or suggest to use a non-linear function to analyze this relationship.

The present claims capture a useful aspect of analysis that is neither taught or suggested by either cited reference. Use of a non-linear function arises from an understanding that amplification efficiency of a PCR reaction varies with initial nucleic acid concentration and in fact varies in a non-linear fashion with low concentrations of initial nucleic acid. Lowe *et al.* does not appear to even understand that amplification efficiency is important and, as the Examiner acknowledges, does not describe this aspect.

Zhang *et al.*, on the other hand, does make a correlation between cycle threshold and initial nucleic acid concentration, but if anything, teaches that the correlation is linear. For example, Figures 1B and 1D graphs the relationship of cycle threshold and log of initial concentration as a straight line. Zhang *et al.* clearly assume that the correlation is linear. This teaching, if anything, *teaches away* from using a non-linear function to analyze the correlation, and thus teaches away from the claimed subject matter.

It is also noteworthy that Zhang *et al.* go out of their way to state that the "exactness of the ... standard curves is not a critical part of the method described herein...." (Zhang *et al.*, col. 9, lines 15-19). This statement suggests that there is no need to investigate further and is further evidence that Zhang *et al.* assume that a linear function is adequate to analyze amplification efficiency.

In sum, the Examiner has not indicated where or how the cited art taught or suggested the use of a non-linear function to analyze cycle threshold and initial nucleic acid concentration. In fact, neither of the cited references teach or suggest the use of a non-linear function to analyze cycle threshold and initial nucleic acid concentration. Accordingly, the Examiner has not set forth a *prima facie* obviousness rejection.

In view of the arguments above, Applicants respectfully request withdrawal of the rejection.

B. Claims 17 and 36-37

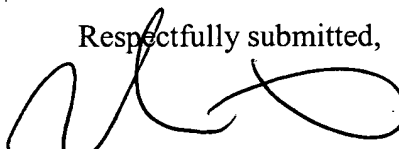
The Examiner also rejected claims 17 and 36-37 as allegedly obvious over Lowe *et al.* in view of Zhang *et al.* and Wittwer *et al.* The rejection assumed that the independent claims were obvious in view of the Lowe and Zhang references. As discussed above, the independent claims are not obvious. The addition of the Wittwer reference does nothing to cure this defect. Therefore, withdrawal of the rejection is requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



Matthew E. Hinsch
Reg. No. 47,651

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 415-576-0200
Fax: 415-576-0300
Attachments
MEH:meh